REMARKS

I. Claim Changes

The scope of the claims, especially method-of-preservation claim 10 and composition claim 21, has been broadened by the above changes after a review of the cited references, especially Shimono and Greenspan, which suggests that previous analysis of the subject matter of these references has not considered certain important differences between their subject matter and that of the claimed invention.

II. Objection to the Disclosure

The disclosure in the specification was objected to because the subject matter of claim 21 was not described in the originally filed specification.

A sentence has been added to next to last paragraph on page 4 of the specification, which describes cosmetic preparations applied to the skin. This sentence states that no organic chemical preservatives are present in these preparations, especially those preservatives that produce cytotoxic and allergenic reactions when applied to the skin.

The last two paragraphs on page 4 of the applicants' specification now completely support all the features of the amended claim 21. Note that the upper limit of 25 wt. % for the bioactive glass appears in the last paragraph on page 4.

Basis for the changes in the next to last paragraph on page 4 of the applicants' specification is present in the originally filed specification, which does not have section headings (because the subject matter is not clearly divided into such sections). First note that the "object of the invention" on page 2, next to last full paragraph, states that the object is to provide a preservative agent, which exerts no negative application effects, especially when applied to the skin, in contrast to previously known agents. The preservative agents that cause cytotoxic and allergenic reactions are described as organo-chemical preservatives, i.e. organic chemical preservatives, in the second and third paragraph on page 1 of applicants' specification. This provides a basis for excluding the organic chemical preservatives from the cosmetic and/or pharmaceutical preparations containing bioactive glass.

For the foregoing reasons and because of the changes in the paragraph in the specification on page 4, withdrawal of the objection to the disclosure is respectfully requested.

III. Indefiniteness Rejection

Claims 13 and 19 were rejected under 35 U.S.C. 112, second paragraph, as indefinite.

Claims 13 and 19 have been amended in accordance with the suggestion on pages 3 and 4 of applicants' specification. These claims have been amended to state that the bioactive glass contains at least one toxic metal cation but in

amounts such that toxic amounts of the at least one toxic metal cation are not released. This puts an upper limit on the amount of the toxic metal cation or cations that are present in the bioactive glass using functional language. Functional wording is acceptable in patent claims according to M.P.E.P. 2173.05 (g).

The fourth full paragraph on page 4 of the applicants' specification provides a basis for this wording change in claims 13 and 19.

For the foregoing reasons and because of the changes in claims 13 and 19, withdrawal of the rejection of amended claims 13 and 19 under 35 U.S.C. 112, second paragraph, is respectfully requested.

IV. Provisional Double Patenting Rejections

Claims 10 to 15 were *provisionially* rejected under the judicially created doctrine of obviousness-type double patenting (ODP) as obvious over claims 14 to 18, 64 to 68 and 70 of copending U.S. Patent Application, Ser. No. 09/818,466, inventors, Lee, et al.

Similarly claims 16 to 24 were provisionially rejected under the judicially created doctrine of obviousness-type double patenting (ODP) as obvious over claims 1 to 5, 59 to 63, 69, 92 to 93 and 122 to 123 of copending U.S. Patent Application, Ser. No. 09/818,466, inventors, Lee, et al.

A signed terminal disclaimer, which has been prepared in accordance with 37 C.F.R. 1.130 (b) to overcome these ODP rejections, accompanies this

amendment and is signed by undersigned attorney of record. The subject matter of the present application and copending U.S. Patent Application, Ser. No. 09/818,466, are commonly owned 100 % by Schott AG and were so commonly owned at the time the present application was filed in the U.S.P.T.O.

The terminal disclaimer disclaims that portion of the term of any patent that issues on the present application that exceeds the expiration date of the patent that issues in the copending U.S. Patent Application, Ser. No. 09/818,466, subject to the qualifications made in the terminal disclaimer (that the present application and the copending application continue to be commonly owned, etc).

For the foregoing reasons and especially because of the signed terminal disclaimer filed with this amendment, withdrawal of the ODP rejections of claims 10 to 15 and 16 to 24 as unpatentable over the above-stated claims of copending U.S. Patent Application, Ser. No. 09/818,466, is respectfully requested.

V. Anticipation Rejection based on Shimono, et al

Claims 10 to 14 and 21 to 24 were rejected under 35 U.S.C. 102 (b) as anticipated by U.S. Patent 5,290,544 to Shimono, et al.

Shimono, et al, do disclose a soluble glass containing silver ions, which can be used as a preservative for cosmetic preparations. Particle sizes of the soluble glass are from 420 to 600 microns (abstract, claim 1). Examples are provided in columns 3 to 6 of this U.S. Patent. The soluble glass can be either a borosilicate glass or a phosphate glass, according to column 1, lines 54 to 56.

Examples of the composition of the soluble glass are provided at column 3, lines 41 to 43; column 4, lines 27 to 28; column 6, lines 28 to 29; and column 7, lines 20 to 23, as well as claims 3 to 6 of U.S. '544.

Basically the soluble glass of Shimono is a delivery vehicle for silver ions, which have been used since biblical times to preserve food and drink (column 2, lines 3 to 14). Silver cans were used by Alexander the Great to transport water for his army during their conquering marches, because of the antibacterial and antimicrobial action of silver. Of course this is well before the issue date of U.S. '544.

However the soluble glass disclosed by Shimono is **not** bioactive glass. First, this reference does not characterize the soluble glass as bioactive glass and the term "bioactive glass" does not appear anywhere in the reference.

The soluble glass used by Shimono would not have any antimicrobial action after all the toxic cations, especially after all of the silver ions, have been released from it. In the case of applicants' claimed method and preparations the bioactive glass has an antimicrobial action on its own without the toxic metal cations. Furthermore preferred embodiments of applicants' claimed method and preparations employ a bioactive glass that does not contain either silver ions or other toxic metal cations, like copper or zinc ions.

Thus the issue here is the scope of the term "bioactive glass" and it is respectfully submitted that this term does not encompass any of the soluble glass materials disclosed either in general in Shimono, et al, or in the examples in columns 3 to 6 of Shimono, et al.

Bioactive glass is defined in prior art references, some of which are cited in applicants' specification, for example U.S. Patent 5,074,916, issued December 24, 1991. In the 'Description of the Prior art' section of this patent it states that bioactive glass must contain a substantial amount of both sodium oxide and calcium oxide as well as phosphorus oxide in addition to SiO_2. It must have a comparatively high ratio of calcium to phosphorus. Shimono states that the soluble glass can be a borosilicate glass or a phosphate glass, but Shimono never discloses that the phosphate glass must include SiO_2, Na_2O and CaO. None of the examples in columns 3 to 8 contain all four required ingredients. The four ingredients are necessary to provide the bioactive glass material itself with its characteristic properties.

Also applicants' specification defines "bioactive glass". For example see the two full paragraphs on page 3 of applicants' specification. These paragraphs state that bioactive glass must at least contain SiO_2, calcium ions and phosphate ions as well as at least one other element from the group sodium potassium, etc. and especially high amounts of Na_2O.

Shimono, et al, never disclose a soluble glass composition that one can identify as containing SiO_2, calcium ions and phosphate ions and sodium oxide. Thus the soluble glass of Shimono, et al, is not a bioactive glass. Especially the soluble glasses of Shimono, et al, do not form a hydroxyl apatite layer so that they can e.g. form an interfacial bond with bone without releasing toxic cations.

It is well established that each and every limitation of a claimed invention must be disclosed in a single prior art reference in order to be able to reject the

claimed invention under 35 U.S.C. 102 (b) based on the disclosures in the single prior art reference. See M.P.E.P. 2131 and also the opinion in ***In re Bond***, 15 U.S.P.Q. 2nd 1566 (Fed. Cir.1990).

Since Shimono, et al, do not disclose a bioactive glass or a method of preserving a preparation with bioactive glass (since the soluble glass of Shimiono is not bioactive glass), none of claims 10 to 14 and 21 to 24 can be rejected as anticipated by Shimono, et al.

In view of the new analysis of the subject matter of Shimono, et al, claims 10 and 21 have been broadened by the above changes, since applicants should be entitled to broader patent claim coverage.

For the foregoing reasons withdrawal of the rejection of amended claims 10 to 14 and 21 to 24 under 35 U.S.C. 102 (b) as anticipated by Shimono, et al, is respectfully requested.

VI. Obviousness Rejection based on Shimono, et al, and Greenspan

Claims 15 and 20 were rejected under 35 U.S.C. 103 (a) over U.S. Patent 5,290,544 issued to Shimono, et al, in view of International Patent Application WO 98/11853 filed by Greenspan.

Shimono, et al, has been discussed in more detail above in connection with the anticipation rejection. Shimono, et al, do not disclose a method of preserving a cosmetic and/or pharmaceutical composition by adding bioactive glass because the soluble glass of Shimono, et al, is not a bioactive glass. The

soluble glass of Shimono, et al, would not provide any antibacterial or antimicrobial action without the addition of the toxic ions, such as silver ion. This is in stark contrast to a bioactive glass which can provide safe antimicrobial action without the assistance of toxic metal cations.

A bioactive glass according to the prior art references cited in applicants' specification and also the description of bioactive glass in applicants' specification must contain a substantial amount of both sodium oxide and calcium oxide as well as phosphorus oxide in addition to SiO_2. Also it must have a comparatively high ratio of calcium to phosphorus. The soluble glass of Shimono, et al, does not include all these required ingredients.

Greenspan discloses a composition for accelerated healing of wounds comprising bioactive glass particles and at least one topical antibiotic and a method for accelerating healing of wounds using the composition (see claims 1, 2 and 9 of Greenspan). Claim 2 of Greenspan does disclose a bioactive glass composition containing silicon dioxide, calcium oxide, sodium oxide and phosphorous oxide as required ingredients, which is consistent with the above regarding bioactive glass. However Greenspan does not disclose or suggest that the bioactive glass has antimicrobial or antibacterial action, but instead discloses other functions for the bioactive glass (see page 12, lines 10 and following). The antibiotic or antimicrobial action in the composition of Greenspan is provided by the topical antibiotic, for example the antibiotics recited in claim 6 of Greenspan, including tetracycline, bacitracin, gentamicin, etc.

More specifically, Greenspan, in a lengthy background section, explains

that the healing of a wound is a cascade process, in which blood cells coagulate in a first phase and wound repair is initiated as an inflammatory response in the a second phase. Infection is controlled by the inflammatory response as described in the second paragraph on page 3 of Greenspan. Page 12, line 16 and following, explains that the natural immune responses of the body are activated by various growth factors implicated in tissue repair. The activation of the growth factors is catalyzed by the presence of the bioactive glass. Also the development of the phosphate layer on the bioactive glass in the presence of water containing fluids attracts collagen, fibronectin and cells to the wound, which speeds up the healing process.

Thus the bioactive glass has the effect of speeding up the basic chemical reactions and transport processes that comprise the healing process according to Greenspan. Greenspan does not suggest that the bioactive glass has an antibacterial or antimicrobial action itself, but instead requires that the composition used to heal the wounds includes an antibiotic, as explained on page 13, in order to provide antimicrobial action.

It is well established by many U. S. Court decisions that to reject a claimed invention under 35 U.S.C. 103 there must be some hint or suggestion in the prior art of the modifications of the disclosure in a prior art reference or references used to reject the claimed invention, which are necessary to arrive at the claimed invention. For example, the Court of Appeals for the Federal Circuit has said:

> "Rather, to establish obviousness based on a combination of elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was

made by the applicant...Even when obviousness is based on as single reference there must be a showing of a suggestion of motivation to modify the teachings of that reference.." ***In re Kotzab***, 55 U.S.P.Q. 2nd 1313 (Fed. Cir. 2000). See also M.P.E.P. 2141

In the case of instant method claim 15 for a method of preserving a perishable composition with the bioactive glass according to Greenspan having the composition according to claim 2 of Greenspan, Greenspan does not suggest modification of the method of preserving Shimono, et al, by replacing the toxic-metal-cation-containing soluble glass of Shimono, et al (which is not bioactive glass), with the bioactive glass of Greenspan, et al. The reason is simply that Greenspan, et al, does not disclose that the bioactive glass of claim 2 of that reference has antimicrobial or antibiotic activity itself. Greenspan, et al, teaches that the bioactive glass has different functions and does not mention any antimicrobial action. Greenspan, in short, does not suggest the modifications of Shimono, et al, necessary to arrive at the invention claimed in method claim 15.

If Greenspan suggests anything it would be including the antibiotic, such as NEOSPORIN®, in the preservative comprising the silver ion-containing soluble glass of Shimono, which would not occur for several reasons not discussed further here. However that would not lead to the claimed invention.

Regarding the composition according to claim 20, note that all the features and limitations of independent claim 16 are part of the subject matter of claim 20, because claim 20 depends on it.

Neither reference suggests anything regarding whether or not alcohol is

present in the cosmetic or pharmaceutical composition. The subject matter of claim 20 is limited to cosmetic preparations that do not contain alcohol, since it depends on claim 16.

There is no suggestion of the negative limitation that the composition does not contain alcohol in either Shimono, et al, or Greespan. Some of the antibiotics of claim 6 of Greenspan are alcohols. Also example 3 of Shimono (column 6) discloses a face power that includes the soluble glass preservative, but also ethanol and glycerol. Thus Shimono, et al, **teach against** this negative limitation because they teach that their soluble glass preservative can be included in cosmetic compositions including alcohol.

More importantly, there is no suggestion in Greenspan that any of the soluble glass particulates in the cosmetic preparations of Shimono, et al, should be replaced by bioactive glass. The bioactive glass of Greenspan performs different functions from the soluble glass of Shimono, et al.

For the foregoing reasons withdrawal of the rejection of claims 15 and 20 under 35 U.S.C. 103 (a) over U.S. Patent 5,290,544 issued to Shimono, et al, in view of International Patent Application WO 98/11853 filed by Greenspan, is respectfully requested.

VII. Obviousness Rejection based on Shimono and Various Scientific Journal Articles

Claims 16 to 19 were rejected under 35 U.S.C. 103 (a) over U.S. Patent 5,290,544 issued to Shimono, et al, in view of Yamanaka, et al, Chem. Materials

4(3), pp. 495-497 (1992); Wu, et al, Chem. Materials 5(1), pp. 115 - 120 (1993); and Wang, et al., Anal. Chem. 65 (19), pp. 2671- 2675 (1993).

Shimono, et al, has been discussed in greater detail above. Shimono, et al, do not disclose a method of preserving a cosmetic and/or pharmaceutical composition by adding bioactive glass because the soluble glass of Shimono, et al, is not bioactive glass. The soluble glass of Shimono, et al, would not provide any antibacterial or antimicrobial action without the addition of the toxic ions, such as silver ion. This is in stark contrast to a bioactive glass which can provide safe antimicrobial action without the assistance of toxic metal cations.

Furthermore bioactive glass must contain a substantial amount of both sodium oxide and calcium oxide as well as phosphorus oxide in addition to SiO_2. It must have a comparatively high ratio of calcium to phosphorus. The soluble glass of Shimono, et al, does not contain all of these required ingredients, which are necessary to provide antimicrobial action without toxic metal cations.

The secondary references do not supply the necessary hint or suggestion to prepare a glass matrix or a glass particulate with a composition comprising SiO_2, CaO, Na_2O and P_2O_5, with a comparatively large Ca to P ratio. These references all disclose formation of silica-containing sol-gel glass matrices including biomolecules. The biomolecules are incorporated in a silica gel matrix, which does not necessarily include any of the other ingredients, namely CaO, Na_2O and P_2O_5, which characterize a bioactive glass.

For example see the preparation procedure for the sol-glass matrix in the left hand column on page 2672 of Wang, et al., Anal. Chem. 65 (19), pp. 2671-

2675 (1993). In this procedure TMOS (tetramethyloxysilane) and water are mixed with acid (HCl) and stirred to obtain a silica sol. Then fluorescein and antifluorescein, which is an antibody, were immediately added to the silica sol. Then the resulting mixture is allowed to gel, to form the sol-gel glass samples, whose emission spectra are measured.

First, the result sol-gel does not contain the required ingredients of a bioactive glass. Especially it does not contain large amounts of CaO. Also this reference does not provide any general hints or suggestions to include CaO in the sol-gel glass matrix containing the biomolecules, in this case antibodies.

The same procedure for making a sol-gel glass matrix is described in the other references. For example, see the "Experimental Section" of Wu, et al, Chem. Materials 5(1), pp. 115 - 120 (1993) and line 17, left hand column, page 496 of Yamanaka, et al, Chem. Materials 4(3), pp. 495-497 (1992). None of these references provide the necessary hint or suggestion to prepare a sol-gel glass matrix with large amounts of CaO in comparison to P_2O_5. They do not suggest a glass with the required ingredients for bioactive glass.

Furthermore none of these references suggest a two-phase cosmetic composition comprising liquid and bioactive glass particles, as claimed in claim 16. Claim 16 requires that the liquid (usually a water solution in the case of typical cosmetic compostions) does not contain alcohol and contains bioactive glass particles with an index of refraction that at least nearly matches that of the liquid cosmetic compositions. When that is the case the glass particles essentially disappear from view.

Furthermore the references only disclose sol-gel matrices, not two-phase compositions, one phase of which is a liquid in which the bioactive glass particulate is suspended. For example, lines 8 to 12, of the right hand column of page 495 of Yamanaka, et al, Chem. Materials 4(3), pp. 495-497 (1992) disclose that the product sol-gel matrix is a "silicate glass monolith with dimensions 10 mm x 5 mm x 2 mm". In other words, the silicate is in the surrounding gel matrix (a solid), and is not present in glass particles, which are suspended in a liquid.

It is true that the secondary references do disclose a transparent silicate glass (the sol-gel glass matrix), for example, Yamada, et al, p, 496. However if the silicate glass monolith, which has an index of refraction of around 1.8, were ground into glass particles and dispersed in water with an index of refraction around 1 (which the secondary references do not disclose or suggest), the resulting glass particles would be clearly visible in the water because of the difference in index of refraction. However if the same glass particulate were added to an oil with an index of refraction around 1.8, the glass particles would not be visible. The main concept of claim 16 is that the composition of the bioactive glass is adjusted by changing amounts of optional oxides or one or more of the ingredients so that the index of refraction of the glass particulate matches the liquid medium. This feature is not disclosed or suggested in Shimono, et al, or any of the secondary references.

The secondary references do *not* disclose a bioactive glass particulate, particularly a glass particulate with a particles size less than or equal to 400 microns. One skilled in the bioactive glass art would not consider the disclosures

in these secondary references as relevant to either applicants' claimed invention or the preservative disclosed by Shimono, et al. The secondary references would not be combined with the primary reference; they are not reasonably pertinent to the disclosures in the primary reference, Shimono, et al.

Thus none of the secondary references suggest the modifications of the primary reference, Shimono, et al, which are necessary to obtain the claimed invention.

For the foregoing reasons withdrawal of the rejection of claims 16 to 19 under 35 U.S.C. 103 (a) over U.S. Patent 5,290,544 issued to Shimono, et al. in view of Yamanaka, et al, Chem. Materials 4(3), pp. 495-497 (1992); Wu, et al, Chem. Materials 5(1), pp. 115 - 120 (1003); and Wang, et al., Anal. Chem. 65 (19), pp. 2671- 2675 (1993) is respectfully requested.

Should the Examiner require or consider it advisable that the specification, claims and/or drawing be further amended or corrected in formal respects to put this case in condition for final allowance, then it is requested that such amendments or corrections be carried out by Examiner's Amendment and the case passed to issue. Alternatively, should the Examiner feel that a personal discussion might be helpful in advancing the case to allowance, he or she is invited to telephone the undersigned at 1-631-549 4700.

In view of the foregoing, favorable allowance is respectfully solicited.

Respectfully submitted,

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